Getting better visualization of joint cartilage through cationic CT contrast agents

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In its quest to find new strategies to treat osteoarthritis and other diseases, a Boston University-led research team has reported finding a new computer tomography contrast agent for visualizing the special distributions of glycosaminoglycans (GAGs) - the anionic sugars that account for the strength of joint cartilage.

Assessing the local variations in GAGs are of significant interest for the study of cartilage biology and for the diagnosis of cartilage disease like osteoarthritis, which afflicts more than 27 million in people in the United States

In their research paper, "Effect of Contrast Agent Change on Visualization of Articular Cartilage Using Computer Tomography: Exploiting Electrostatic Interactions for Improved Sensitivity," just published on line in the *Journal of the American Chemical Society,* they describe new contrast agents that selectively bind to the GAGs in articular cartilage.

Articular or joint cartilage is the smooth hydrated tissue in the ends of bones in load-bearing joints, such as knees, hips and shoulders. The loss of GAGs from these joints is the hallmark of osteoarthritis, a degenerative joint disease in which wear or trauma results in damage to the cartilage surface.

To better see the differentiation between healthy and unhealthy cartilage, contrast agents provide the visual tool to assess GAG content. However,

the current contrast agents used with computer tomography or magnetic resonance imaging (MRI) rely on limited diffusion of the anionic or negative ion-charged contrast agents into the target tissue, the study noted.

So researchers hypothesized that cationic contrast agents would be electrostatically attracted to anionic GAGs to provide a more sensitive technique for imaging cartilage. And they focused on using the more widely accessible CT equipment because it can image cartilage and bone simultaneously, enable rapid three-dimensional reconstruction of the tissue and achieve higher spatial resolution over shorter acquisition times compared to MRI systems.

The team synthesized three cationic or positive ion-charged iodine-based X-ray contrast agents. Using the femur of a rabbit, they reported gaining better and more specific images for the cartilage tissue than with current negative ion-charged contrast agents.

"Compared to commercially available contrast agents under the same experimental conditions, these new cationic agents are three times more sensitive for imaging cartilage," said Mark W. Grinstaff, Boston University Professor of Chemistry and Biomedical Engineering who led the team with Brian D. Snyder, MD, Ph.D. an orthopedic surgeon at Children's Hospital and Harvard Medical School.

Snyder noted that the ability to acquire information about localized GAG content, morphology and cartilage thickness on tissue samples will, in the future, aid in the diagnosis and treatment of osteoarthritis.

And while the data presented a compelling case for continued development of cationic CT contrast agents, the research team cautioned that the suitability for in vivo applications remains to be determined, adding that toxicity levels and radiation dosage will be the focus of

future studies.

"However, the ability to characterize ex vivo cartilage samples is clearly evident," the study concludes. "Currently obtaining data about the spatial distribution of biochemical components in tissue samples is largely accomplished using histology, which is destructive and time consuming, and thus the use of contrast agents in conjunction with CT imaging will result in readily available, nondestructive alternative to histology."

Source: Boston University Medical Center